Nitrate and Nitrite

Symbol:	**NO_3 / NO_2**
Molecular Weight:	**62 / 46**

What Are They? Nitrate and nitrite are compounds that contain a nitrogen atom joined to oxygen atoms, with nitrate containing three oxygen atoms and nitrite containing two. In nature, nitrates are readily converted to nitrites and vice versa. Both are anions, or ions with a negative charge. They tend to associate with cations, or ions with a positive charge, to achieve a neutral charge balance.

How Are They Used? Nitrates are primarily used to make fertilizer; they are also used in making glass and explosives and other chemical production and separation processes. Nitrites are manufactured mainly for use as a food preservative, and both nitrates and nitrites are used extensively to enhance the color and extend the shelf life of processed meats.

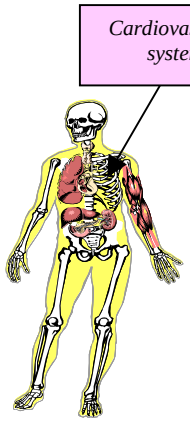
What's in the Environment? Nitrates are naturally present in soil, water, and food. In the natural nitrogen cycle, bacteria convert nitrogen to nitrate, which is taken up by plants and incorporated into plant tissues. Animals that eat plants use the nitrate to produce proteins. Nitrate is returned to the environment in animal feces, as well as through microbial degradation of plants and animals after they die.

Microorganisms can convert nitrate or the ammonium ion (which is a nitrogen atom combined with four hydrogen atoms) to nitrite; this reaction occurs in the environment as well as within the digestive tract of humans and other animals. After bacteria convert (or reduce) nitrate to nitrite in the environment, the nitrogen cycle is completed when they then convert the nitrite to nitrogen. Normally, this natural cycling process does not allow excessive amounts of nitrates or nitrites to accumulate in the environment. However, human activities have increased environmental nitrate concentrations, with agriculture being the major source. This includes increased use of nitrogen-containing fertilizers as well as concentrated livestock and poultry farming; the latter two produce millions of tons of nitrate-containing manure each year. Nitrate and nitrite compounds are very soluble in water and mobile in the environment. They have a high potential for entering surface water when it rains, as excess rainwater flows into streams or lakes; they also have a high potential for entering groundwater through leaching. The concentration associated with soil particles has been estimated to be about half the concentration in interstitial water (the water in the pore spaces between the soil particles).

What Happens to It in the Body? Nitrate is a normal component of the human diet, with the average daily intake from all sources estimated at 75 milligrams (mg), or about 0.0026 ounces. Upon ingestion, about 5% of the nitrate taken in by healthy adults is converted (reduced) to nitrite by bacteria in saliva. Further nitrate is converted by bacteria inside the alimentary tract. (In contrast to nitrates, nitrites are not found naturally in the environment at significant levels.) Certain conditions in the stomach can increase the conversion of nitrate to nitrite, specifically when the pH of the gastric fluid is high enough (above 5) to favor the growth of nitrate-reducing bacteria. This process is of major concern for infants, because their gastrointestinal system normally has a higher pH. Nitrites in the stomach can react with food proteins to form N-nitroso compounds; these compounds can also be produced when meat containing nitrites or nitrates is cooked, particularly using high heat. While these compounds are carcinogenic in test animals, evidence is inconclusive regarding their potential to cause cancer (such as stomach cancer) in humans.

What Are the Primary Health Effects? Nitrates themselves are relatively nontoxic. However, when swallowed, they are converted to nitrites that can react with the hemoglobin in the blood, oxidizing the divalent iron in hemoglobin to the trivalent form and creating methemoglobin. This methemoglobin cannot bind oxygen, which decreases the capacity of the blood to transport oxygen so less oxygen is transported from the lungs to the body tissues, thus causing a condition known as methemoglobinemia.

Normal individuals have naturally low levels (0.5 to 2%) of methemoglobin in their blood. When this level increases to 10%, the skin and lips can takes on a bluish tinge (cyanosis), and levels above 25% can cause weakness and a rapid pulse. At levels above 50 to 60% a person can lose consciousness, go into a coma, and die. Infants are much more sensitive to nitrates/nitrites, and essentially all deaths from nitrate/nitrite poisoning have been in infants.



Primary system affected when nitrate/nitrite is ingested.

What Are the Risks? The Environmental Protection Agency (EPA) has developed toxicity values to estimate the risk of non-cancer health effects from ingesting nitrates and nitrites. The toxicity value used to estimate a non-cancer effect is called a reference dose (RfD). An RfD is an estimate of the highest dose that can be taken in every day without causing an adverse effect. These values have been developed from studies of test animals together with information available for humans exposed to nitrates and/or nitrites and considering sensitive subgroups, notably infants.

The RfD for nitrate was developed considering the concentration at which methemoglobinemia was indicated at levels >10% for 0 to 3-month old infants. This was based on a daily intake of formula made with water containing 10 mg per liter (mg/L) of nitrate as nitrogen. (This reflects the amount of nitrogen within a nitrate molecule, where 1 mg nitrate as nitrogen = 4.4 mg nitrate as measured in the water.) Most cases of infant methemoglobinemia are associated with exposure to formula prepared with drinking water at nitrate-nitrogen levels at least two times higher, or >20 mg/L nitrate-nitrogen. For nitrite, the RfD is based on a 10-kg (22-pound [lb]) child drinking 1 liter, or about 1 quart, of water every day. The RfD represents a "safe daily dose" and so is compared to the amount an individual is estimated to take in every day, as a ratio. No adverse effects have been linked with inhaling nitrates or nitrites, so no inhalation RfDs have been developed. The contribution of nitrites, and indirectly nitrates, to potential human carcinogenicity and the magnitude of the associated risk are unclear. Nitrites react with secondary amines in food to form nitrosamines, many of which are carcinogenic in experimental animals and exert other toxic effects. While the EPA has not developed slope factors (toxicity values used to estimate cancer risk) for nitrates or nitrites, some are available for nitrosamines.

Chemical Toxicity Values	
Non-Cancer Effect	
Oral RfD: NO_3	***Oral RfD: NO_2***
1.6 mg/kg-day	0.1 mg/kg-day

What Are the Current Limits for Environmental Releases and Human Exposure? The EPA requires that sodium nitrite releases of more than 100 lb (45.4 kg) and nitrate releases of more than 10,000 lb (4,540 kg) be immediately reported for inclusion in the nationwide Toxics Release Inventory. The limit for nitrosamines ranges from 1 to 10 pounds. The primary drinking water standards for nitrate and nitrite are 10 and 1 parts per million (ppm), respectively. The Food and Drug Administration allows these compounds to be used as food additives as long as they are of food grade and are added only in the amount needed. The maximum amount of nitrite allowed in smoked and cured fish and meat is 200 ppm.

Where Can I Find More Information? More information on nitrates and nitrates can be found in the primary information sources used to prepare this overview: (1) Consumer Fact Sheet on Nitrates/Nitrites, EPA Office of Groundwater and Drinking Water, available through http://www.epa.gov/OGWDW/dwh/c-ioc/nitrates.html; (2) the EPA's Integrated Risk Information System, http://www.epa.gov/iris/subst/0076.htm (nitrate) and /0078.htm (nitrite); and (3) the National Library of Medicine Hazardous Substances Data Bank (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB).